II. Amendments to Claims 1, 11-13 and 14-15 and Cancelled Claim 13

Claim 1 has been amended to limit the neuromuscular conditions set forth in claim 1 to dystonia. Claim 11 has been amended to make it consistent with claim 1. Claim 12 has been amended to limit dystonia to cervical dystonia. Finally, the dependencies of claims 14 and 15 have been amended.

Applicants hereby cancel claim 13 without prejudice to further prosecution at a later date.

III. The Section 112(1) Rejection

The Office Action rejected claims 1 and 11-15 under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement.

Thus, page 2 of the Office Action states that "The claims contain subject matter which is not described in the specification in such a way as to enable one skilled in the art to which it pertains or with which it is most nearly connected to make and/or use the invention."

Additionally, page 3 of the Office Action states that the specification does not "provide the essential information necessary to practise the claimed method, such as knowledge of the route, duration, and quantity of administration of botulinum type B"

The rest of the Office Action is in the same vein, reiterating that the specification does not contain sufficient disclosure so as to enable claims directed to use of a botulinum toxin type B.

Hence, the basis of the rejection is (as alleged by the Office Action) that the specification does not teach how to use a botulinum toxin type B in the claimed method. The Office Action does not allege that there is insufficient teaching in the specification regarding use of a botulinum toxin type A, or as to any other aspect of the claimed invention. Hence, it is the narrow issue as to the extent of the guidance provided by the specification regarding use of a botulinum toxin type B in the claimed methods upon which the rejection in the Office Action entirely rests.

Significantly, all claims, as amended, in this application are limited to use of at least about 80 units of a botulinum toxin type B in a patient with a dystonia, so as

to treat the dystonia, after the patient has experienced a loss of clinical response to a botulinum toxin type A.

Respectfully, the rejection is in error and should be withdrawn because the specification contains ample teaching of the claimed use of a botulinum toxin type B. For example:

1. "The term botulinum toxin is a generic term embracing the family of toxins...given the designations A, B, C, D, E, F and G" (specification page 2, lines 24-29)

2. Pages 4-5 of the specification explain that for various reasons a patient being treated with a botulinum toxin type A can develop a lack of clinical responsiveness to further injections of the botulinum toxin type A. It is then disclosed at page 5, lines 12-15 of the specification that a botulinum toxin type B can then be used, according to the present invention.

3. Pages 5-6 of the specification discloses that various dystonias (such as "focal dystonias such as spasmodic torticollis can be treated with a botulinum toxin type B after a lack of clinical response has developed to administration of a botulinum toxin type A. See page 5, lines 19- 28 and page 6, lines 1-6 of the specification. See also page 7, lines 4-8 and 26-28 of the specification, which disclose use of a botulinum toxin type B after a botulinum toxin type A. As is well known, "spasmodic torticollis" is a synonym for "cervical dystonia."

4. Page 9, lines 31-35 of the specification, continuing to page 10, lines 1 3, discloses that the toxins (including therefore botulinum toxin type B) used in the invention, can be administered by intramuscular injection or by subcutaneous injection. Thus, the specification does disclose the route of administration of the botulinum toxin type B.

5. Page 9, lines 31-35 of the specification, continuing to page 10, lines 1 3, discloses that the toxins used in the invention (i.e. botulinum toxins type A and B) can be administered by injection "into a spastic muscle" or "directly to the affected muscle region". Thus, the specification does disclose the location of the botulinum toxin type B administration.

6. Page 10, lines 33-35 of the specification discloses that "The dose of toxin administered to the patient will depend upon the severity of the condition; e.g., the number of muscle groups requiring treatment, the age and size of the patient and, the potency of the toxin" Furthermore, page 11, lines 8-15 of the specification explicitly discloses particular units amounts of toxin to be administered, and the relevant units amounts as disclosed here (80 units) are set forth in the claims with regard to botulinum toxin type B. Thus, the specification does disclose the dose to use of a botulinum toxin type B.

7. Page 12, lines 24-29 of the specification discloses the absence of side effects when the claimed method is practiced. Hence, the efficacy of use of the botulinum toxin type B is disclosed by the specification.

8. Example 2 on pages 14-15 of the specification discloses clinical use of a botulinum toxin type B to treat cervical dystonia (spasmodic torticollis).

Note that all claims have been limited to use of a specific amount of a botulinum toxin type B in the treatment of the specific condition dystonia, which has become unresponsive to treatment with botulinum toxin type A.

As set forth above, the specification does disclose the route of administration, location of administration, dosage, efficacy and clinical use of botulinum toxin type B to treat cervical dystonia. Hence, the 35 U.S.C. §112(1) rejection of the claims should be withdrawn.

IV. Conclusion

All issues raised by the Office Action have been addressed. Examination and allowance of claims 1 and 11-12 and 14-15 is requested.

Respectfully Submitted,

Date: September 9, 2003

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CERTIFICATE OF EXPRESS MAILING UNDER 37 C.F.R. §1.10

I hereby certify that this Transmittal Letter, the response to the Office Action and the documents referred to as enclosed herein are being deposited with the United States Postal Service on September 9, 2003 in an envelope as "Express Mail Post Office To Addressee" mailing label number EV295682355US with sufficient postage for Express Mail addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

Susan Bartholomew
Name of Person mailing paper

Date: September 9, 2003

Signature of person mailing paper

THE CLAIMS

1. (currently amended) A method of treating a patient suffering from a ~~neuromuscular disorder or condition wherein the neuromuscular disorder or condition is selected from the group consisting of: disorders of ocular motility;~~ dystonias~~; tremors; tics; segmental myoclonus; spasms; spasticity; tension headache; levator pelvic syndrome; spina bifida, tardive dyskinesia; Parkinson's disease and; stuttering~~, the method comprising intramuscular or subcutaneous administration to the patient of up to 1,000 units of a botulinum toxin type A per patient treatment session until the patient experiences loss of clinical response to the administered botulinum toxin type A, as determined by a failure of the administered botulinum toxin type A to achieve a marked reduction of or to substantially alleviate a symptom of the dystonia~~neuromuscular disorder or condition~~, and thereafter administering to the patient at least about 80 units of a botulinum toxin type B to thereby again achieve a marked reduction or a substantial alleviation of a symptom of the dystonia~~neuromuscular disorder or condition being treated~~.

11. (currently amended). The method of claim 1, wherein the dystonia~~neuromuscular disorder or condition~~ is cervical dystonia

12. (currently amended) A method of treating cervical dystonia in a patient, the method comprising intramuscular or subcutaneous administration to a patient with dystonia of up to 1,000 units of a botulinum toxin type A per patient treatment session until the patient experiences loss of clinical response to the administered botulinum toxin type A, as determined by a failure of the administered botulinum toxin type A to achieve a marked reduction of a symptom of the cervical dystonia, and thereafter administering to the patient at least about 80 units of a botulinum toxin type B.

13. (cancelled)

14. (currently amended) The method of claim 1~~2~~3, wherein treating the cervical dystonia reduces the severity of an abnormal head position symptom of the cervical dystonia.

15. (currently amended) The method of claim 1~~3~~2, wherein treating the cervical dystonia reduces a neck pain associated with the cervical dystonia.